respectfully request that the Examiner enter new Claim 100 (submitted herewith) and consider the following remarks.

IN THE CLAIMS

**The amendments to Claims 12 and 31 as well as the new claims (Claims 45-99) which were filed with Applicants' previous reply of October 28, 2002 are reproduced below for the Examiner's convenience. Additionally, please enter new Claim 100.**

12. (Amended) A method for screening a candidate compound for the ability to reduce cellular proliferation comprising the steps of:

(a) providing a sublethal level of an antisense nucleic acid complementary to at least a portion of a nucleic acid encoding a gene product in a cell to reduce the activity or amount of said gene product in said cell, thereby producing a sensitized cell, wherein said gene product is a gene product whose activity or amount is reduced by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 521, 1390, 1463, 1845, 2782 and 3283;

(b) contacting said sensitized cell with a compound; and

(c) determining the degree to which said compound inhibits proliferation of said sensitized cell relative to a nonsensitized cell.

31. (Amended) A method for screening a candidate compound for the ability to reduce cellular proliferation comprising:

(a) providing a sublethal level of an antisense nucleic acid complementary to at least a portion of a nucleic acid encoding a gene product in a cell to reduce the activity or amount of said gene product in said cell, thereby producing a sensitized cell, wherein said gene product is selected from the group consisting of a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs: 521, 1390, 1463, 1845, 2782 and 3283, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is

inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 521, 1390, 1463, 1845, 2782 and 3283, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 521, 1390, 1463, 1845, 2782 and 3283 under stringent conditions, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 521, 1390, 1463, 1845, 2782 and 3283 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOs: 521, 1390, 1463, 1845, 2782 and 3283;

(b) contacting said sensitized cell with a compound; and

(c) determining the degree to which said compound inhibits the growth of said sensitized cell relative to a nonsensitized cell.

45. (New) The method of Claim 31, wherein said determining step comprises determining whether said compound inhibits the growth of said sensitized cell to a greater extent than said compound inhibits the growth of said nonsensitized cell.

46. (New) The method of Claim 31, wherein said gene product is from an organism other than *E. coli*.

47. (New) The method of Claim 31, wherein said cell is an organism other than *E. coli*.

48. (New) The method of Claim 31, wherein said sensitized cell is an organism selected from the group consisting of *Anaplasma marginale, Aspergillus fumigatus, Bacillus anthracis, Bacterioides fragilis Bordetella pertussis, Burkholderia cepacia, Campylobacter jejuni, Candida albicans, Candida glabrata (also called Torulopsis glabrata), Candida tropicalis, Candida parapsilosis, Candida guilliermondii, Candida krusei, Candida kefyr (also called Candida pseudotropicalis), Candida dubliniensis, Chlamydia pneumoniae, Chlamydia trachomatus, Clostridium botulinum, Clostridium difficile, Clostridium perfringens, Coccidiodes immitis, Corynebacterium diptheriae, Cryptococcus neoformans, Enterobacter cloacae, Enterococcus faecalis, Enterococcus faecium, Escherichia coli, Haemophilus influenzae,*

*Helicobacter pylori, Histoplasma capsulatum, Klebsiella pneumoniae, Listeria monocytogenes, Mycobacterium leprae, Mycobacterium tuberculosis, Neisseria gonorrhoeae, Neisseria meningitidis, Nocardia asteroides, Pasteurella haemolytica, Pasteurella multocida, Pneumocystis carinii, Proteus vulgaris, Pseudomonas aeruginosa, Salmonella bongori, Salmonella cholerasuis, Salmonella enterica, Salmonella paratyphi, Salmonella typhi, Salmonella typhimurium, Staphylococcus aureus, Listeria monocytogenes, Moxarella catarrhalis, Shigella boydii, Shigella dysenteriae, Shigella flexneri, Shigella sonnei, Staphylococcus epidermidis, Streptococcus pneumoniae, Streptococcus mutans, Treponema pallidum, Yersinia enterocolitica, Yersinia pestis* and any species falling within the genera of any of the above species.

49. (New) The method of Claim 31, wherein said sensitized cell is a Gram positive bacterium.

50. (New) The method of Claim 49, wherein said Gram positive bacterium is selected from the group consisting of *Staphylococcus* species, *Streptococcus* species, *Enterococcus* species, *Mycobacterium* species, *Clostridium* species, and *Bacillus* species.

51. (New) The method of Claim 50, wherein said bacterium is *Staphylococcus aureus*.

52. (New) The method of Claim 50, wherein said *Staphylococcus* species is coagulase negative.

53. (New) The method of Claim 51, wherein said bacterium is selected from the group consisting of *Staphylococcus aureus* RN450 and *Staphylococcus aureus* RN4220.

54. (New) The method of Claim 31, wherein said antisense nucleic acid is transcribed from an inducible promoter.

55. (New) The method of Claim 31, further comprising the step of contacting said cell with a concentration of inducer which induces transcription of said antisense nucleic acid to a sublethal level.

56. (New) The method of Claim 31, wherein growth inhibition is measured by monitoring optical density of a culture medium.

57. (New) The method of Claim 31, wherein said gene product is a polypeptide.

58. (New) The method of Claim 57, wherein said polypeptide comprises a polypeptide selected from the group consisting of a polypeptide having at least 99% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide selected from the group consisting of SEQ ID NOs.: 5021, 5283, 10251, 10689, 10969, 11370, 11955, 12600, 13518 and 13703 and a polypeptide whose activity may be complemented by a polypeptide selected from the group consisting of SEQ ID NOs: 5021, 5283, 10251, 10689, 10969, 11370, 11955, 12600, 13518 and 13703.

59. (New) The method of Claim 57, wherein said polypeptide comprises a polypeptide selected from the group consisting of a polypeptide having at least 95% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide selected from the group consisting of SEQ ID NOs.: 5021, 5283, 10251, 10689, 10969, 11370, 11955, 12600, 13518 and 13703 and a polypeptide whose activity may be complemented by a polypeptide selected from the group consisting of SEQ ID NOs: 5021, 5283, 10251, 10689, 10969, 11370, 11955, 12600, 13518 and 13703.

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60. (New) The method of Claim 57, wherein said polypeptide comprises a polypeptide selected from the group consisting of a polypeptide having at least 90% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide selected from the group consisting of SEQ ID NOs.: 5021, 5283, 10251, 10689, 10969, 11370, 11955, 12600, 13518 and 13703 and a polypeptide whose activity may be complemented by a polypeptide selected from the group consisting of SEQ ID NOs: 5021, 5283, 10251, 10689, 10969, 11370, 11955, 12600, 13518 and 13703.

61. (New) The method of Claim 57, wherein said polypeptide comprises a polypeptide selected from the group consisting of a polypeptide having at least 85% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide selected from the group consisting of SEQ ID NOs.: 5021, 5283, 10251, 10689, 10969, 11370, 11955, 12600, 13518 and 13703 and a polypeptide whose activity may be complemented by a polypeptide selected from the group consisting of SEQ ID NOs: 5021, 5283, 10251, 10689, 10969, 11370, 11955, 12600, 13518 and 13703.

62. (New) The method of Claim 57, wherein said polypeptide comprises a polypeptide selected from the group consisting of a polypeptide having at least at least 80%

amino acid identity as determined using FASTA version 3.0t78 to a polypeptide selected from the group consisting of SEQ ID NOs.: 5021, 5283, 10251, 10689, 10969, 11370, 11955, 12600, 13518 and 13703 and a polypeptide whose activity may be complemented by a polypeptide selected from the group consisting of SEQ ID NOs: 5021, 5283, 10251, 10689, 10969, 11370, 11955, 12600, 13518 and 13703.

63. (New) The method of Claim 57, wherein said polypeptide comprises a polypeptide selected from the group consisting of a polypeptide having at least 70% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide selected from the group consisting of SEQ ID NOs.: 5021, 5283, 10251, 10689, 10969, 11370, 11955, 12600, 13518 and 13703 and a polypeptide whose activity may be complemented by a polypeptide selected from the group consisting of SEQ ID NOs: 5021, 5283, 10251, 10689, 10969, 11370, 11955, 12600, 13518 and 13703.

64. (New) The method of Claim 57, wherein said polypeptide comprises a polypeptide selected from the group consisting of a polypeptide having at least 60% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide selected from the group consisting of SEQ ID NOs.: 5021, 5283, 10251, 10689, 10969, 11370, 11955, 12600, 13518 and 13703 and a polypeptide whose activity may be complemented by a polypeptide selected from the group consisting of SEQ ID NOs: 5021, 5283, 10251, 10689, 10969, 11370, 11955, 12600, 13518 and 13703.

65. (New) The method of Claim 57, wherein said polypeptide comprises a polypeptide selected from the group consisting of a polypeptide having at least 50% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide selected from the group consisting of SEQ ID NOs.: 5021, 5283, 10251, 10689, 10969, 11370, 11955, 12600, 13518 and 13703 and a polypeptide whose activity may be complemented by a polypeptide selected from the group consisting of SEQ ID NOs: 5021, 5283, 10251, 10689, 10969, 11370, 11955, 12600, 13518 and 13703.

66. (New) The method of Claim 57, wherein said polypeptide comprises a polypeptide selected from the group consisting of a polypeptide having at least 40% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide selected from the group consisting of SEQ ID NOs.: 5021, 5283, 10251, 10689, 10969, 11370, 11955, 12600, 13518 and

13703 and a polypeptide whose activity may be complemented by a polypeptide selected from the group consisting of SEQ ID NOs: 5021, 5283, 10251, 10689, 10969, 11370, 11955, 12600, 13518 and 13703.

67. (New) The method of Claim 57, wherein said polypeptide comprises a polypeptide selected from the group consisting of a polypeptide having at least 25% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide selected from the group consisting of SEQ ID NOs.: 5021, 5283, 10251, 10689, 10969, 11370, 11955, 12600, 13518 and 13703 and a polypeptide whose activity may be complemented by a polypeptide selected from the group consisting of SEQ ID NOs: 5021, 5283, 10251, 10689, 10969, 11370, 11955, 12600, 13518 and 13703.

68. (New) The method of Claim 57, wherein said polypeptide is selected from the group consisting of 5021, 5283, 10251, 10689, 10969, 11370, 11955, 12600, 13518 and 13703.

69. (New) The method of Claim 57, wherein said polypeptide comprises a polypeptide selected from the group consisting of a polypeptide having at least 34% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide having SEQ ID NO: 12600, a polypeptide having at least 39% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide having SEQ ID NO: 12600, a polypeptide having at least 42% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide having SEQ ID NO: 12600 and a polypeptide having at least 43% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide having SEQ ID NO: 12600.

70. (New) The method of Claim 57, wherein said polypeptide comprises a polypeptide selected from the group consisting of a polypeptide having at least 32% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide having SEQ ID NO: 10689, a polypeptide having at least 33% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide having SEQ ID NO: 10689, a polypeptide having at least 37% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide having SEQ ID NO: 10689, a polypeptide having at least 63% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide having SEQ ID NO: 10689 and a polypeptide having at least 77% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide having SEQ ID NO: 10689.

71. (New) The method of Claim 31, wherein said nucleic acid encoding said gene product comprises a nucleic acid selected from the group consisting of a nucleic acid comprising a nucleic acid having at least 97% nucleic acid identity as determined using BLASTN version 2.0 with the default parameters to a sequence selected from the group consisting of SEQ ID NOS.: 3966, 4228, 6154, 6592, 6872, 7273, 7857, 8502, 9420 and 9605, a nucleic acid which hybridizes to a sequence selected from the group consisting of SEQ ID NOS.: 3966, 4228, 6154, 6592, 6872, 7273, 7857, 8502, 9420 and 9605 under stringent conditions, and a nucleic acid which hybridizes to a sequence selected from the group consisting of SEQ ID NOS.: 3966, 4228, 6154, 6592, 6872, 7273, 7857, 8502, 9420 and 9605 under moderate conditions.

72. (New) The method of Claim 31, wherein said nucleic acid encoding said gene product comprises a nucleic acid selected from the group consisting of a nucleic acid comprising a nucleic acid having at least 95% nucleic acid identity as determined using BLASTN version 2.0 with the default parameters to a sequence selected from the group consisting of SEQ ID NOS.: 3966, 4228, 6154, 6592, 6872, 7273, 7857, 8502, 9420 and 9605, a nucleic acid which hybridizes to a sequence selected from the group consisting of SEQ ID NOS.: 3966, 4228, 6154, 6592, 6872, 7273, 7857, 8502, 9420 and 9605 under stringent conditions, and a nucleic acid which hybridizes to a sequence selected from the group consisting of SEQ ID NOS.: 3966, 4228, 6154, 6592, 6872, 7273, 7857, 8502, 9420 and 9605 under moderate conditions.

73. (New) The method of Claim 31, wherein said nucleic acid encoding said gene product comprises a nucleic acid selected from the group consisting of a nucleic acid comprising a nucleic acid having at least 90% nucleic acid identity as determined using BLASTN version 2.0 with the default parameters to a sequence selected from the group consisting of SEQ ID NOS.: 3966, 4228, 6154, 6592, 6872, 7273, 7857, 8502, 9420 and 9605, a nucleic acid which hybridizes to a sequence selected from the group consisting of SEQ ID NOS.: 3966, 4228, 6154, 6592, 6872, 7273, 7857, 8502, 9420 and 9605 under stringent conditions, and a nucleic acid which hybridizes to a sequence selected from the group consisting of SEQ ID NOS.: 3966, 4228, 6154, 6592, 6872, 7273, 7857, 8502, 9420 and 9605 under moderate conditions.

74. (New) The method of Claim 31, wherein said nucleic acid encoding said gene product comprises a nucleic acid selected from the group consisting of a nucleic acid comprising a nucleic acid having at least 85% nucleic acid identity as determined using BLASTN version 2.0

with the default parameters to a sequence selected from the group consisting of SEQ ID NOS.: 3966, 4228, 6154, 6592, 6872, 7273, 7857, 8502, 9420 and 9605, a nucleic acid which hybridizes to a sequence selected from the group consisting of SEQ ID NOS.: 3966, 4228, 6154, 6592, 6872, 7273, 7857, 8502, 9420 and 9605 under stringent conditions, and a nucleic acid which hybridizes to a sequence selected from the group consisting of SEQ ID NOS.: 3966, 4228, 6154, 6592, 6872, 7273, 7857, 8502, 9420 and 9605 under moderate conditions.

75. (New) The method of Claim 31, wherein said nucleic acid encoding said gene product comprises a nucleic acid selected from the group consisting of a nucleic acid comprising a nucleic acid having at least 80% nucleic acid identity as determined using BLASTN version 2.0 with the default parameters to a sequence selected from the group consisting of SEQ ID NOS.: 3966, 4228, 6154, 6592, 6872, 7273, 7857, 8502, 9420 and 9605, a nucleic acid which hybridizes to a sequence selected from the group consisting of SEQ ID NOS.: 3966, 4228, 6154, 6592, 6872, 7273, 7857, 8502, 9420 and 9605 under stringent conditions, and a nucleic acid which hybridizes to a sequence selected from the group consisting of SEQ ID NOS.: 3966, 4228, 6154, 6592, 6872, 7273, 7857, 8502, 9420 and 9605 under moderate conditions.

76. (New) The method of Claim 31, wherein said nucleic acid encoding said gene product comprises a nucleic acid selected from the group consisting of a nucleic acid comprising a nucleic acid having at least 70% nucleic acid identity as determined using BLASTN version 2.0 with the default parameters to a sequence selected from the group consisting of SEQ ID NOS.: 3966, 4228, 6154, 6592, 6872, 7273, 7857, 8502, 9420 and 9605, a nucleic acid which hybridizes to a sequence selected from the group consisting of SEQ ID NOS.: 3966, 4228, 6154, 6592, 6872, 7273, 7857, 8502, 9420 and 9605 under stringent conditions, and a nucleic acid which hybridizes to a sequence selected from the group consisting of SEQ ID NOS.: 3966, 4228, 6154, 6592, 6872, 7273, 7857, 8502, 9420 and 9605 under moderate conditions.

77. (New) The method of Claim 31, wherein said nucleic acid encoding said gene product is selected from the group consisting of 3966, 4228, 6154, 6592, 6872, 7273, 7857, 8502, 9420 and 9605.

78. (New) The method of Claim 31, wherein said antisense nucleic acid comprises a nucleic acid having at least 97% nucleotide sequence identity to a nucleotide sequence selected

from the group consisting of one of the sequences of SEQ ID NOS. 521, 1390, 1463, 1845, 2782 and 3283.

79. (New) The method of Claim 31, wherein said antisense nucleic acid comprises a nucleic acid having at least 95% nucleotide sequence identity to a nucleotide sequence selected from the group consisting of one of the sequences of SEQ ID NOS. 521, 1390, 1463, 1845, 2782 and 3283.

80. (New) The method of Claim 31, wherein said antisense nucleic acid comprises a nucleic acid having at least 90% nucleotide sequence identity to a nucleotide sequence selected from the group consisting of one of the sequences of SEQ ID NOS. 521, 1390, 1463, 1845, 2782 and 3283.

81. (New) The method of Claim 31, wherein said antisense nucleic acid comprises a nucleic acid having at least 85% nucleotide sequence identity to a nucleotide sequence selected from the group consisting of one of the sequences of SEQ ID NOS. 521, 1390, 1463, 1845, 2782 and 3283.

82. (New) The method of Claim 31, wherein said antisense nucleic acid comprises a nucleic acid having at least 80% nucleotide sequence identity to a nucleotide sequence selected from the group consisting of one of the sequences of SEQ ID NOS. 521, 1390, 1463, 1845, 2782 and 3283.

83. (New) The method of Claim 31, wherein said antisense nucleic acid comprises a nucleic acid having at least 70% nucleotide sequence identity to a nucleotide sequence selected from the group consisting of one of the sequences of SEQ ID NOS. 521, 1390, 1463, 1845, 2782 and 3283.

84. (New) The method of Claim 31, wherein said antisense nucleic acid comprises a nucleic acid having at least 70% nucleotide sequence identity to a nucleotide sequence comprising at least 100 consecutive nucleotides of a nucleotide sequence selected from the group consisting of SEQ ID NOs: 521, 1390, 1463, 1845, 2782 and 3283.

85. (New) The method of Claim 12, wherein said determining step comprises determining whether said compound inhibits the growth of said sensitized cell to a greater extent than said compound inhibits the growth of said nonsensitized cell.

86. (New) The method of Claim 12, wherein said gene product is from an organism other than *E. coli*.

87. (New) The method of Claim 12, wherein said cell is an organism other than *E. coli*.

88. (New) The method of Claim 12, wherein said sensitized cell is an organism selected from the group consisting of *Anaplasma marginale, Aspergillus fumigatus, Bacillus anthracis, Bacterioides fragilis Bordetella pertussis, Burkholderia cepacia, Campylobacter jejuni, Candida albicans, Candida glabrata (also called Torulopsis glabrata), Candida tropicalis, Candida parapsilosis, Candida guilliermondii, Candida krusei, Candida kefyr (also called Candida pseudotropicalis), Candida dubliniensis, Chlamydia pneumoniae, Chlamydia trachomatus, Clostridium botulinum, Clostridium difficile, Clostridium perfringens, Coccidiodes immitis, Corynebacterium diptheriae, Cryptococcus neoformans, Enterobacter cloacae, Enterococcus faecalis, Enterococcus faecium, Escherichia coli, Haemophilus influenzae, Helicobacter pylori, Histoplasma capsulatum, Klebsiella pneumoniae, Listeria monocytogenes, Mycobacterium leprae, Mycobacterium tuberculosis, Neisseria gonorrhoeae, Neisseria meningitidis, Nocardia asteroides, Pasteurella haemolytica, Pasteurella multocida, Pneumocystis carinii, Proteus vulgaris, Pseudomonas aeruginosa, Salmonella bongori, Salmonella cholerasuis, Salmonella enterica, Salmonella paratyphi, Salmonella typhi, Salmonella typhimurium, Staphylococcus aureus, Listeria monocytogenes, Moxarella catarrhalis, Shigella boydii, Shigella dysenteriae, Shigella flexneri, Shigella sonnei, Staphylococcus epidermidis, Streptococcus pneumoniae, Streptococcus mutans, Treponema pallidum, Yersinia enterocolitica, Yersinia pestis* and any species falling within the genera of any of the above species.

89. (New) The method of Claim 12, wherein said sensitized cell is a Gram positive bacterium.

90. (New) The method of Claim 89, wherein said Gram positive bacterium is selected from the group consisting of *Staphylococcus* species, *Streptococcus* species, *Enterococcus* species, *Mycobacterium* species, *Clostridium* species, and *Bacillus* species.

91. (New) The method of Claim 90, wherein said bacterium is *Staphylococcus aureus*.

92. (New) The method of Claim 90, wherein said *Staphylococcus* species is coagulase negative.

93. (New) The method of Claim 91, wherein said bacterium is selected from the group consisting of *Staphylococcus aureus* RN450 and *Staphylococcus aureus* RN4220.

94. (New) The method of Claim 12, wherein said antisense nucleic acid is transcribed from an inducible promoter.

95. (New) The method of Claim 12, further comprising the step of contacting said cell with a concentration of inducer which induces transcription of said antisense nucleic acid to a sublethal level.

96. (New) The method of Claim 12, wherein growth inhibition is measured by monitoring optical density of a culture medium.

97. (New) The method of Claim 12, wherein said gene product is a polypeptide.

98. (New) The method of Claim 97, wherein said polypeptide is selected from the group consisting of 5021, 5283, 10251, 10689, 10969, 11370, 11955, 12600, 13518 and 13703.

99. (New) The method of Claim 12, wherein said nucleic acid encoding said gene product is selected from the group consisting of 3966, 4228, 6154, 6592, 6872, 7273, 7857, 8502, 9420 and 9605.

100. (New) A method for screening a candidate compound for the ability to reduce cellular proliferation comprising the steps of:

(a) providing a sublethal level of an antisense nucleic acid selected from the group consisting of SEQ ID NOs: 521, 1390, 1463, 1845, 2782 and 3283, wherein said antisense nucleic acid reduces the activity or amount of a gene product required for cellular proliferation, thereby producing a sensitized cell;

(b) contacting said sensitized cell with a compound; and

(c) determining the degree to which said compound inhibits proliferation of said sensitized cell relative to a nonsensitized cell.

## REMARKS

As Applicants explained in their reply filed October 28, 2002, Claims 12 and 31 have been amended to broaden their scope. New claims 45-84, which are dependent on claim 31, and